Hybrid multiscale modelling of multiple myeloma development, impact on erythropoiesis, intraclonal heterogeneity, and treatment

Anass Bouchnita

Laboratoire de Biométrie et Biologie Evolutive (LBBE),
CNRS 5558, University Lyon 1, Villeurbanne, France

Abstract:

Multiple myeloma (MM) is a genetically complex hematological cancer characterized by the infiltration of the bone marrow by malignant myeloma cells. As in other types of cancer, MM evolves from a benign malignancy to a more aggressive one by natural selection in an evolutionary process. This progression is characterized by the acquisition of sequential changes involving many genes, resulting in the emergence of aggressive plasma clones. The survival and growth of each of these clones depend on the intra-clonal competition for a limited panel of cytokines available in the tumor site. MM causes anemia by impairing eyrhtopoiesis and, thus, downregulating the production of red blood cells. While the progression of MM can be partially controlled by chemotherapeutic agents, such treatments become toxic when administrated in high doses. Multiscale models in biology are developed by integrating data across different biological scales of space and time in order to study different physiological systems. Cell population systems are usually described using hybrid discrete continuous models. In such models, cells are represented as individual objects that move, divide, die by apoptosis, and interact with each other. These actions are determined by intracellular and extracellular regulation mechanisms described by continuous models. In this talk, we briefly discuss the different applications of hybrid and multiscale models in biology and, in particular, tumor growth. Next, we present a hybrid multiscale model describing the normal functioning of erytropoiesis and its response to anemia. Then, we study the development of MM and its intraclonal heterogeneity in order to understand its impact on erythropoiesis. In this context, a data-driven modelling approach is used to quantify the impact of MM on erythropoiesis during different chemotherapeutic treatment regimens. We conclude by discussing the important role of Darwinian evolution in cancer progression and how mathematical modelling provides key insights in understanding its underlying mechanism.

References:

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